Figure **5** shows the islet containing process fluid flow in forward direction through the digestion chamber during pancreatic digestion, islet separation, and process fluid circulation **309**, shown in (previously described in Fig. **1** and Fig. **4**) according to one preferred embodiment of the invention. The process solution flows through the dynamic flow digestion chamber **120** in the forward direction while process valves **116**, **180**, and **126** are open and process valves **115**, **117**, **125**, and **127** are closed. Process fluid flow through the dynamic flow digestion chamber **120** (previously described in Fig. **1** and Fig. **4**) in the reverse direction is achieved while process valves **115**, **125**, **180**, **117**, and **127** are open and process valves **116** and **126** are closed.

All publications, patents, and patent documents are incorporated herein by reference, as though individually incorporated by reference. The invention has been described with reference to various specific and preferred embodiments and techniques. However, it should be understood that many variations and modifications might be made while remaining within the spirit and scope of the invention. The above descriptions of exemplary embodiments are for illustrative purposes. Because of variations that will be apparent to those skilled in the science, the present invention is not intended to be limited to the particular embodiments described above. Thus, various modifications of the above-described embodiments will be apparent to those skilled in the science. The present invention may also be practiced in the absence of any element not specifically disclosed. The invention may be uniformly applied to islets of Langerhans containing insulin producing beta cells harvested from animals and mammals either transgenic or non-transgenic. The scope of the invention is defined by the following claims.

CLAIMS

What is claimed is:

1. A method of isolating islets from a pancreas where the physiologic islet processing solution temperature is a controlled process variable and is controlled via setpoint by a microprocessor temperature controller.

2. The method of claim 1 wherein the physiologic islet processing fluid temperature is controlled between 36 °C and 42 °C.

3. The method of claim 1 wherein the islet processing fluid temperature is controlled between 0 to 36 °C and 42 to 50 °C.

4. The method of claim 1 wherein the controller is a microprocessor process controller.

5. The method of claim 2 wherein the controller is a microprocessor process controller.

6. The method of claim 3 wherein the controller is a microprocessor process controller.

7. The method of claim 1 wherein the controller is a microprocessor computer.

8. The method of claim 2 wherein the controller is a microprocessor computer.

9. The method of claim 3 wherein the controller is a microprocessor computer.

10. The method of claim 1 wherein the controller is a programmable logic controller.

11. The method of claim 2 wherein the controller is a programmable logic controller.

12. The method of claim 3 wherein the controller is a programmable logic controller.

13. The method of claim 1 wherein the controller is a variable resistance transformer.

14. The method of claim 2 wherein the controller is a variable resistance transformer.

15. The method of claim 3 wherein the controller is a variable resistance transformer.

16. The method of claim 1 wherein the controller is a solid-state electronic relay device.

17. The method of claim 2 wherein the controller is a solid-state electronic relay device.

18. The method of claim 3 wherein the controller is a solid-state electronic relay device.

19. The method of claim 1 wherein the process temperature is automatically controlled.

20. The method of claim 2 wherein the process temperature is automatically controlled.

21. The method of claim 3 wherein the process temperature is automatically controlled.

22. The method of claim 1 wherein the pancreas is derived from a transgenic biological source.

23. The method of claim 2 wherein the pancreas is derived from a transgenic biological source.

24. The method of claim 3 wherein the pancreas is derived from a transgenic biological source.

25. The method of claim 1 wherein the pancreas is derived from a non-transgenic biological source.

26. The method of claim 2 wherein the pancreas is derived from a non-transgenic biological source.

27. The method of claim 3 wherein the pancreas is derived from a non-transgenic biological source.

28. A method of isolating islets from a pancreas where the physiologic islet processing solution percent hydrogen concentration (pH) is a controlled process variable and is controlled via setpoint by a microprocessor pH controller.

29. The method of claim 28 wherein the physiologic islet processing fluid pH is controlled between 6.5 pH and 8.0 pH.

30. The method of claim 28 wherein the physiologic islet processing fluid pH is controlled between 0 pH to 6.5 pH and 8.0 pH to 14 pH.

31. The method of claim 28 wherein the controller is a microprocessor process controller.

32. The method of claim 29 wherein the controller is a microprocessor computer.

34. The method of claim 30 wherein the controller is a microprocessor computer

35. The method of claim 28 wherein the controller is a programmable logic controller.

36. The method of claim 29 wherein the controller is a programmable logic controller.

37. The method of claim 30 wherein the controller is a programmable logic controller

38. The method of claim 28 wherein the controller is a solid-state electronic relay device.

39. The method of claim 29 wherein the controller is a solid-state electronic relay device.

40. The method of claim 30 wherein the controller is a solid-state electronic relay device.

41. The method of claim 28 wherein the process pH is automatically controlled.

42. The method of claim 29 wherein the process pH is automatically controlled.

43. The method of claim 30 wherein the process pH is automatically controlled.

44. The method of claim 28 wherein the pancreas is derived from a transgenic biological source.

45. The method of claim 29 wherein the pancreas is derived from a transgenic biological source.

46. The method of claim 30 wherein the pancreas is derived from a transgenic biological source.

47. The method of claim 28 wherein the pancreas is derived from a non-transgenic biological source.

48. The method of claim 29 wherein the pancreas is derived from a non-transgenic biological source.

49. The method of claim 30 wherein the pancreas is derived from a non-transgenic biological source.

50. A method of isolating islets from a pancreas where the physiologic islet processing solution dissolved oxygen concentration (DO) is a controlled process variable and is controlled via setpoint by a microprocessor DO controller.

51. The method of claim 50 wherein the physiologic islet processing fluid DO is controlled between 0.001 mol/ml DO and 0.1 mol/ml DO.

52. The method of claim 50 wherein the physiologic islet processing fluid DO is controlled between 0.001 mol/ml DO and 0.1 mol/ml DO.

53. The method of claim 50 wherein the controller is a microprocessor process controller.

54. The method of claim 51 wherein the controller is a microprocessor process controller.

55. The method of claim 52 wherein the controller is a microprocessor process controller.

56. The method of claim 50 wherein the controller is a microprocessor computer.

67. The method of claim 51 wherein the controller is a microprocessor computer.

58. The method of claim 52 wherein the controller is a microprocessor computer.

59. The method of claim 50 wherein the controller is a programmable logic controller.

60. The method of claim 51 wherein the controller is a programmable logic controller.

61. The method of claim 52 wherein the controller is a programmable logic controller.

62. The method of claim 50 wherein the controller is a solid-state electronic relay device.

63. The method of claim 39 wherein the controller is a solid-state electronic relay device.

64. The method of claim 50 wherein the controller is a solid-state electronic relay device.

65. The method of claim 50 wherein the process DO is automatically controlled.

66. The method of claim 51 wherein the process DO is automatically controlled.

67. The method of claim 52 wherein the process DO is automatically controlled.

68. The method of claim 50 wherein the pancreas is derived from a transgenic biological source.

69. The method of claim 51 wherein the pancreas is derived from a transgenic biological source.

70. The method of claim 52 wherein the pancreas is derived from a transgenic biological source.

71. The method of claim 50 wherein the pancreas is derived from a non-transgenic biological source.

72. The method of claim 51 wherein the pancreas is derived from a non-transgenic biological source.

73. The method of claim 52 wherein the pancreas is derived from a non-transgenic biological source.

74. A method of isolating islets from a pancreas where the physiologic islet processing solution flowrate is a controlled process variable and is controlled via setpoint by a microprocessor flow controller.

75. The method of claim 74 wherein the physiologic islet processing fluid flowrate is controlled between 20 ml/min flowrate 2000 ml/min flowrate.

76. The method of claim 74 wherein the physiologic islet processing fluid flowrate is controlled between 0 ml/min to 20 ml/min flowrate and 2000 ml/min to 20000 ml/min flowrate.

77. The method of claim 74 wherein the controller is a microprocessor process controller.

78. The method of claim 75 wherein the controller is a microprocessor process controller.

79. The method of claim 76 wherein the controller is a microprocessor process controller.

80. The method of claim 74 wherein the controller is a microprocessor computer.

81. The method of claim 75 wherein the controller is a microprocessor computer.

82. The method of claim 76 wherein the controller is a microprocessor computer.

83. The method of claim 74 wherein the controller is a programmable logic controller.

84. The method of claim 75 wherein the controller is a programmable logic controller.

85. The method of claim 76 wherein the controller is a programmable logic controller.

86. The method of claim 74 wherein the controller is a solid-state electronic relay device.

87. The method of claim 75 wherein the controller is a solid-state electronic relay device.

88. The method of claim 76 wherein the controller is a solid-state electronic relay device.

89. The method of claim 74 wherein the process flowrate is automatically controlled.

90. The method of claim 75 wherein the process flowrate is automatically controlled.

91. The method of claim 76 wherein the process flowrate is automatically controlled.

92. The method of claim 74 wherein the pancreas is derived from a transgenic biological source.

81. The method of claim 75 wherein the pancreas is derived from a transgenic biological source.

93. The method of claim 76 wherein the pancreas is derived from a transgenic biological source.

94. The method of claim 74 wherein the pancreas is derived from a non-transgenic biological source.

95. The method of claim 75 wherein the pancreas is derived from a non-transgenic biological source.

96. The method of claim 76 wherein the pancreas is derived from a non-transgenic biological source.

97. A method of isolating islets from a pancreas where the physiologic islet processing solution endotoxin concentration is a controlled process variable and is controlled via setpoint by a microprocessor endotoxin controller.

98. The method of claim 97 wherein the physiologic islet processing fluid endotoxin concentration is controlled between 0.00001 EU/ml (endotoxin units/ml) and 0.001 EU/ml.

99. The method of claim 97 wherein the physiologic islet processing fluid endotoxin concentration is controlled between 0.000000001 EU/ml to 0.00001 EU/ml and 0.001 to 10000 EU/ml.

100. The method of claim 97 wherein the controller is a microprocessor process controller.

101. The method of claim 98 wherein the controller is a microprocessor process controller.

102. The method of claim 99 wherein the controller is a microprocessor process controller.

103. The method of claim 97 wherein the controller is a microprocessor computer.

104. The method of claim 98 wherein the controller is a microprocessor computer.

105. The method of claim 99 wherein the controller is a microprocessor computer.

106. The method of claim 97 wherein the controller is a programmable logic controller.

107. The method of claim 98 wherein the controller is a programmable logic controller.

108. The method of claim 99 wherein the controller is a programmable logic controller.

109. The method of claim 97 wherein the controller is a solid-state electronic relay device.

110. The method of claim 98 wherein the controller is a solid-state electronic relay device.

111. The method of claim 99 wherein the controller is a solid-state electronic relay device.

112. The method of claim 97 wherein the process endotoxin concentration is automatically controlled.

113. The method of claim 98 wherein the process endotoxin concentration is automatically controlled.

114. The method of claim 99 wherein the process endotoxin concentration is automatically controlled.

115. The method of claim 97 wherein the pancreas is derived from a transgenic biological source.

116. The method of claim 98 wherein the pancreas is derived from a transgenic biological source.

117. The method of claim 99 wherein the pancreas is derived from a transgenic biological source.

118. The method of claim 97 wherein the pancreas is derived from a non-transgenic biological source.

119. The method of claim 98 wherein the pancreas is derived from a non-transgenic biological source.

120. The method of claim 99 wherein the pancreas is derived from a non-transgenic biological source.

121. The method of automated real-time data acquisition of the process variables that describe the chemical composition of the islet containing physiologic process solution during islet processing defined as the process temperature, or the process percent hydrogen concentration (pH), or the process dissolved oxygen (DO) concentration, or the process flowrate (F), or the process endotoxin concentration (EU), or the process dissolved nitric oxide concentration (NO),

or the process dissolved carbon monoxide concentration (CO), or process dissolved carbon dioxide concentration (CO2), or process proteolytic enzyme concentration (PE), or process antibiotic concentration (A).

122. The method of automatic control of the process variables that describe the chemical composition of the islet containing physiologic process solution during islet processing defined as the process temperature, or the process percent hydrogen concentration (pH), or the process dissolved oxygen (DO) concentration, or the process flowrate (F), or the process endotoxin concentration (EU), or the process dissolved nitric oxide concentration (NO), or the process dissolved carbon monoxide concentration (CO), or process dissolved carbon dioxide concentration (CO2), or process proteolytic enzyme concentration (PE), or process antibiotic concentration (A).

123. The method of claim 121 wherein the pancreas is derived from a transgenic biological source.

124. The method of claim 121 wherein the pancreas is derived from a non-transgenic biological source.

125. The method of claim 122 wherein the pancreas is derived from a transgenic biological source.

126. The method of claim 122 wherein the pancreas is derived from a non-transgenic biological source.

127. The method of claim 121 wherein the data acquisition of the process variables describing the chemical composition of the islet containing physiologic process solution during islet processing is automatic via microprocessor process controllers.

128. The method of claim 122 wherein the data acquisition of the process variables describing the chemical composition of the islet containing physiologic process solution during islet processing is automatic via microprocessor process controllers.

129. The method of claim 121 wherein the control of the process variables describing the chemical composition of the islet containing physiologic process solution during islet processing is automatic via a microprocessor computer.

130. The method of claim 121 wherein the control of the process variables describing the chemical composition of the islet containing physiologic process solution during islet processing is automatic via a programmable logic controller.

132. The method of claim 122 wherein the control of the process variables describing the chemical composition of the islet containing physiologic process solution during islet processing is automatic via a programmable logic controller.

133. The method of claim 121 wherein the control of the process variables describing the chemical composition of the islet containing physiologic process solution during islet processing is automatic via a solid-state electronic relay device.

134. The method of claim 121 wherein the control of the process variables that describe the chemical composition of the islet containing physiologic process solution during islet processing is automatic via a solid-state electronic relay device.

135. The method of deactivating or neutralizing or inhibiting the chemical activity or biologic activity of digestive proteolytic enzymes employed by procedure or from pancreatic tissue in the islet processing solution during automated islet isolation and separation from a pancreas utilizing metal chelators EDTA, or EGTA added to the islet containing physiologic process solution.

136. The method of claim 135 wherein the pancreas is derived from a transgenic biological source.

137. The method of claim 135 wherein the pancreas is derived from a non-transgenic biological source.

138. The method of deactivating or neutralizing or inhibiting the chemical activity or biologic activity of digestive proteolytic enzymes employed by procedure or from pancreatic tissue in the islet processing solution during automated islet isolation and separation from a pancreas utilizing antibiotics cysteine, or tetracycline, or doxycycline, or minocycline added to the islet containing physiologic process solution.

139. The method of claim 138 wherein the pancreas is derived from a transgenic biological source.

140. The method of claim 139 wherein the pancreas is derived from a non-transgenic biological source.

141. The method of deactivating or neutralizing or inhibiting the chemical activity or biologic activity of digestive proteolytic enzymes employed by procedure or from pancreatic tissue in the islet processing solution during automated islet isolation and separation from a pancreas utilizing azo-dyes added to the islet containing physiologic process solution.

142. The method of claim 141 wherein the pancreas is derived from a transgenic biological source.

143. The method of claim 141 wherein the pancreas is derived from a non-transgenic biological source.

144. The method of deactivating or neutralizing or inhibiting the chemical activity or biologic activity of nitric oxide in the islet processing solution during automated islet isolation and separation of islets from a pancreas utilizing cysteine, or tetracycline, or doxycycline or minocycline added to the islet containing physiologic process solution.

145. The method of claim 144 wherein the pancreas is derived from a transgenic biological source.

146. The method of claim 144 wherein the pancreas is derived from a non-transgenic biological source.

147. The method of deactivating or neutralizing or inhibiting the chemical activity or biologic activity of nitric oxide in the islet processing solution during automated islet isolation and separation of islets from a pancreas by reducing the nitric oxide concentration utilizing cysteine, or dextran, or heparin, or cystine added to the islet containing physiologic process solution.

148. The method of claim 147 wherein the pancreas is derived from a transgenic biological source.

149. The method of claim 147 wherein the pancreas is derived from a non-transgenic biological source.

150. The method of deactivating or neutralizing or inhibiting the chemical activity or biologic activity of nitric oxide synthase in the islet processing solution during automated islet isolation and separation of islets from a pancreas by reducing the nitric oxide synthase concentration utilizing cysteine, or dextran, or heparin, or cystine added to the islet containing physiologic process solution.

151. The method of claim 150 wherein the pancreas is derived from a transgenic biological source.

152. The method of claim 150 wherein the pancreas is derived from a non-transgenic biological source.

153. A mechanical and electrical device employed to isolate and separate islets in physiologic process solution during islet processing composed of various electrical or electronic sensors and electrical devices automatically controlled by a microprocessor processor controller.

154. The method of claim 153 wherein the controller is a microprocessor computer..

155. The method of claim 153 wherein the controller is a programmable logic controller.

156. The method of isolation of islets from a pancreas employing a dynamic flow digestion chamber incorporating alternating forward and reverse process fluid flow operating between 2 Hz and 10 KHz.

157. The method of claim 156 wherein the pancreas is derived from a transgenic biological source.

158. The method of claim 156 wherein the pancreas is derived from a non-transgenic biological source.

159. The method of isolation islets from a pancreas employing a dynamic flow digestion chamber incorporating alternating rotary motion to the process fluid flow and the pancreas operating between 0 and 100 rpm (rotations per minute).

160. The method of claim 159 wherein the pancreas is derived from a transgenic biological source.

161. The method of claim 159 wherein the pancreas is derived from a non-transgenic biological source.

162. The method of isolation of islets from a pancreas employing a dynamic flow digestion chamber incorporating self-contained sonic transducers operating between 10 Hz and 100 MHz.

163. The method of claim 162 wherein the pancreas is derived from a transgenic biological source.

164. The method of claim 162 wherein the pancreas is derived from a non-transgenic biological source.

165. The method of claim 156 wherein the digestion chamber is automatically controlled by a microprocessor process controller.

166. The method of claim 156 wherein the digestion chamber is automatically controlled by a microprocessor computer.

167. The method of claim 156 wherein the digestion chamber is automatically controlled by a programmable logic controller.

168. The method of claim 159 wherein the digestion chamber is automatically controlled by a microprocessor process controller.

169. The method of claim 159 wherein the digestion chamber is automatically controlled by a microprocessor computer.

170. The method of claim 159 wherein the digestion chamber is automatically controlled by a programmable logic controller.

171. The method of claim 162 wherein the digestion chamber is automatically controlled by a microprocessor process controller.

172. The method of claim 162 wherein the digestion chamber is automatically controlled by a microprocessor computer.

173. The method of claim 162 wherein the digestion chamber is automatically controlled by a programmable logic controller.

174. A method of isolating islets from a pancreas where the physiologic islet processing solution pressure is a controlled process variable and is controlled via setpoint by a microprocessor temperature controller.

175. The method of claim 174 wherein the physiologic islet processing fluid pressure is controlled between 500 torr and 1000 torr pressure.

176. The method of claim 174 wherein the islet processing fluid pressure is controlled between 100 to 500 torr and 1000 to 10000 torr.

177. The method of claim 174 wherein the controller is a microprocessor process controller.

180. The method of claim 175 wherein the controller is a microprocessor process controller

181. The method of claim 176 wherein the controller is a microprocessor process controller

182. The method of claim 174 wherein the controller is a microprocessor computer.

183. The method of claim 17 5wherein the controller is microprocessor computer.

184. The method of claim 176 wherein the controller is a microprocessor computer.

185. The method of claim 174 wherein the controller is a programmable logic controller.

186. The method of claim 175 wherein the controller is programmable logic controller.

187. The method of claim 176 wherein the controller is programmable logic controller.

188. The method of claim 174 wherein the pancreas is derived from a transgenic biological source.

189. The method of claim 175 wherein the pancreas is derived from a transgenic biological source.

190. The method of claim 176 wherein the pancreas is derived from a transgenic biological source.

191. The method of claim 174 wherein the pancreas is derived from a non-transgenic biological source.

192. The method of claim 175 wherein the pancreas is derived from a non-transgenic biological source.

193. The method of claim 176 wherein the pancreas is derived from a non-transgenic biological source